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PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) 03-237

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Application Number	Filed
10/805,576	March 19, 2004

First Named Inventor: Jan Weber

Art Unit	Examiner
3774	Alvin J. Stewart

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 29,674
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____

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NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

[x] *Total of 1 forms are submitted.

REASONS FOR REQUESTING PRE-APPEAL REVIEW

1) Status of Claims

Claims 1-2, 4-35 and 37-41 are presently pending in the application. Claims 2, 8, 14 and 32 have been withdrawn. Thus, Claims 1, 4-7, 9-13, 15-31, 33-35 and 37-41 are presented for this Pre-Appeal Review.

2) The Rejection Under 35 U.S.C. §103(a) Over PACETTI in View of SHEU is in Error

The Examiner has rejected Claims 1, 4-7, 9-10, 20-30, 33-34 and 37-41 under 35 §U.S.C. 103(a) on the basis of Pacetti et al (U.S. Patent No. 6,663,662) ("PACETTI") in view of Sheu et al (U.S. Patent No. 5,837,377) ("SHEU"). This rejection is believed to be erroneous and is respectfully traversed.

It is believed that the Examiner has not met his burden of establishing a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claimed features. Also, according to the MPEP in a discussion under Section 2141:

> "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR*, 550 U.S. at ___, 82 USPQ2d at 1396 quoting *In re Kahn,* 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). (emphasis added)

In the first instance, it is important to note that the focus of each of PACETTI and SHEU is very different. PACETTI focuses on controlling the rate of drug release from a medical device such as a stent by using a diffusion barrier. SHEU does not teach or suggest the release of any drug from a polyelectrolyte coating and instead focuses on improving the wettability of polymers, especially those to be used in aqueous environments, for example, with contact lenses. In general and specifically, one skilled in the art would not look to SHEU to find suitable coatings to be used in PACETTI.

PACETTI discloses a metallic stent carrying a therapeutic or bioactive substance and having a diffusion barrier to reduce the rate at which the therapeutic or bioactive substance is released. The diffusion barrier comprises a polymeric material impregnated with particles.

In contrast to PACETTI the present invention requires:

> (b) a multilayer coating region comprising multiple polyelectrolyte layers deposited over said surface wherein each polyelectrolyte layer has a net charge opposite in sign from the adjacent layers; and (c) a therapeutic agent disposed within the depressions beneath said multilayer coating region
> (excerpt from Claim 1) (emphasis added)

The Examiner agrees that PACETTI neither teaches nor suggests polyelectrolyte layers covering a stent. As a corollary to this point, PACETTI also does not disclose a therapeutic agent disposed within the depressions beneath said multilayer coating region comprising polyelectrolyte layers. The Examiner then looks to SHEU in order to fill in these deficiencies.

SHEU focuses on improving the wettability of polymers, especially those to be used in aqueous environments, for example, with contact lenses. SHEU teaches hydrophilic articles with a durable hydrophilic coating. It is important to note that SHEU does not teach or suggest:

1) the release of any therapeutic agent from the polyelectrolyte coating; or

2) controlling the rate of release of a therapeutic agent by using a diffusion barrier of the type described in PACETTI.

Thus, both SHEU and PACETTI alone or together fail to teach or suggest a therapeutic agent disposed within the depressions beneath said multilayer coating region comprising polyelectrolyte layers.

Moreover, PACETTI is not even combinable with SHEU for a number of reasons:

First, the Examiner has ignored the effect of the presence of an active ingredient (taught in PACETTI) on the articles of SHEU and the effect of the hydrophilicity requirement of SHEU. In particular, PACETTI notes:

> The presence of an active ingredient in a polymeric matrix typically interferes with the ability of the matrix to adhere effectively to the surface of the device. (see col.7, lines 58-64)

Second, PACETTI does not use a surface treatment. PACETTI clearly states that no surface treatment is needed to retain the coating for its devices (col.16, lines 30-31), while SHEU describes a surface treatment to create an ionic polymeric layer that includes the use of plasma discharge or acid/base chemical modification, or adding the ionic or ionizable groups into the bulk material of the polymer (col. 6, lines 30- 35). None of these methods are used with PACETTI.

Third, in teaching that the "ionically bonded" hydrophilic coatings described in SHEU are durable (e.g., resistant to changes in pH, elevated temperatures, exposure to detergents or organic solvents, abrasion, repeated ultrasonic washings, etc.), SHEU teaches away from the biodisintegrable polyelectrolyte multilayer coating regions claimed in presently pending Claims 4, 12, 13, 15-17, 20, 30 and 40.

Fourth, PACETTI uses solvent systems wherein the amount of solvent is in the range of 59.9-99.8% for the active ingredient coating (col. 8, line 63 – col. 9, line 5). Alternatively, thermoplastic polymers may be used for the primer with heat treating to evaporate the solvent (col. 16, lines 46-64). This approach is in contrast to the technology described in SHEU where a dip-coating method is taught for use with a substrate having an anionic polymer layer by dipping it into a polycationic solution and the method recites that the concentration of the solution cannot exceed 5% (col.7, lines 55-58) at the peril of resulting in non-uniform coatings and increased drying times. The methods of PACETTI on the other hand can tolerate polymer concentrations as high as 35% (col. 8, line 64- col.9, line 5). Thus, the attempted combination of PACETTI and SHEU again fails.

Furthermore, as noted in a previous response, there is no reason why one of ordinary skill in the art would make the articles of PACETTI more hydrophilic, including SHEU's use of hydrogels. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007).

Accordingly, to arrive at the subject matter presently claimed would require, at the very least, undue and impermissible hindsight. See, for example, *Akzo N. V.* v. *U.S. International Trade Commission,* 808 F.2d 1241, 1480-81, 1 USPQ2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied,* 482 U.S. 909 (1987), *Loctite Corp.* v. *Ultraseal Ltd.,* 781 F.2d 861, 874, 228 USPQ 90-99 (Fed. Cir. 1985). See also MPEP 2142, second paragraph.

If the device of PACETTI were modified in accordance with the teachings of SHEU, this would require the creation of an ionic polymeric layer over the diffusion barrier layer of PACETTI, and a disordered polyelectrolyte coating ionically bound to the ionic polymeric layer which would be expected to interfere with, or even prevent, the controlled release of active agent as sought by PACETTI. See *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Thus, while the combination of SHEU with PANCETTI is not taught or suggested, even if one were able to combine PANCETTI with SHEU, the likely result would be a medical device with better wettability on the surface but with an inability to retain the functionality of PACETTI's layer to control the rate of drug diffusion. Thus, there would be no reasonable expectation of success associated with the modification being proposed by the Examiner.

For the reasons described above, Applicant respectfully submits that Claims 1, 4-7, 9-10, 20-30, 33-34 and 37-41 are patentable over the cited references.

3) The Rejection Under 35 U.S.C. §103(a) Over PACETTI in View of SHEU and AMON is in Error

The Examiner has rejected Claims 12, 13 and 15-19 under 35 U.S.C. §103(a) on the basis of PACETTI in view of SHEU and further in view of Amon et al (U.S. Patent No. 5,735,896) ("AMON"). This rejection is believed to be erroneous and is traversed for the reasons described above for PACETTI and SHEU and further for the reasons described herein.

The Examiner agrees that PACETTI does not disclose a stent made of a ceramic surface. The Examiner relies on AMON to provide a teaching of a stent made of metal or ceramic. This rejection is not supportable under the standards cited above. The technology of AMON is completely different than either the technologies of PACETTI or SHEU.

AMON uses semiconductor technology to create an extra strong adherence between an implanted prosthesis and a biocompatible coating. There is no inclusion of a therapeutic agent, and there is no description of any surface depression or pore or any layer placed over a therapeutic agent requiring control of its diffusion rate. Moreover, SHEU's use of hydrophilic layers is not combinable with the semiconductor technology of AMON.

Even if the references were combined, it would still not achieve the present invention. There is no layer with particles as a diffusion modulating layer required by PACETTI and certainly no hydrophilic layers as required by SHEU. It is again noted that SHEU teaches away from biodisintegrable polyelectrolyte multilayer coating regions. AMON's semiconductor technology without the inclusion of any therapeutic agent or any surface depression or pore or any layer placed over a therapeutic agent requiring control of its diffusion rate, in combination with PACETTI and SHEU would not result in the claimed invention and, in fact, are not even combinable.

For the reasons described above, Applicant respectfully submits that Claims 12, 13 and 15-19 are patentable over the cited references.

4) The Rejection Under 35 U.S.C. §103(a) Over PACETTI in View of SHEU and ANDERSON is in Error

The Examiner has rejected Claim 31 under 35 U.S.C. §103(a) on the basis of PACETTI in view of SHEU and further in view of Anderson et al (U.S. Application Publication No. 2005/0172852) ("ANDERSON"). This rejection is believed to be erroneous and is traversed for the reasons described above for PACETTI and SHEU and further for the reasons described herein.

ANDERSON is a reference directed to tattoos. This reference describes technology useful for tissue marking, especially in the art of tattoos. The citation of ANDERSON as a bare disclosure of a metal oxide with a porous surface is not understood and certainly not supportable.

The Examiner refers to paragraph 29 of ANDERSON as disclosing coating a metal oxide in order to have a porous surface. The text of paragraph 29, however, refers to forming a coating, a variable appearance material or an absorption component or mixtures thereof which will absorb electromagnetic radiation. The word "porous" does not even appear in this paragraph.

For the reasons described above, Applicant respectfully submits that Claim 31 is patentable over the cited references.

5) The Rejection Under 35 U.S.C. §103(a) Over HARISH in View of SHEU is in Error

The Examiner has rejected Claim 35 under 35 U.S.C. §103(a) on the basis of Harish et al (U.S. Patent No. 6,506,437) ("HARISH") in view of SHEU. This rejection is believed to be erroneous and is respectfully traversed based on the deficiencies described above for SHEU and further for the reasons described herein.

HARISH discloses a method for coating medical devices having a plurality of "depots" where the depots are filled with a mixture of therapeutic agent and polymer filling the depots. HARISH discloses that when there is a polymeric topcoat, the particulars of the topcoat also control release (col. 10, line 65 - col. 11, line 9).

The Examiner has agreed that HARISH does not disclose "polyelectrolyte layers covering a stent. The Examiner then tries to rely on SHEU but, as has previously been explained, SHEU does not teach or suggest that any therapeutic agents are released from the polyelectrolyte coating. It has also been noted above that SHEU does not teach or suggest that the polyelectrolyte coating is useful to control the release of any bioactive agents. Rather, SHEU discloses medical articles, including contact lenses, having polyelectrolyte coatings for the purpose of rendering them hydrophilic.

Furthermore, if the device of HARISH were modified in accordance with the teachings of SHEU, this would result in the creation of an ionic polymeric layer and a disordered polyelectrolyte coating, which structure is noted in SHEU to be very stable, and which would interfere with, or even prevent, the controlled release of an active agent as taught by HARISH.

With respect to the *method* aspects of Claim 35, the limitations of this claim are not met. In particular, after the polyelectrolyte layer is applied in step (b), the disintegrable material that was placed in the depressions in step (a) is removed in step (c). Only then is the agent added to the depressions in step (d). No method of this nature is taught or suggested in HARISH and/or SHEU.

For at least the reasons discussed above, Applicant respectfully submits that Claim 35 is patentable over the cited references.